L5 ANSWER 11 OF 14 MEDLINE
AN 86042633 MEDLINE
DN 86042633 PubMed ID: 3933002
TI Linkage map of three **HLA-DR beta**-chain genes: evidence for a recent duplication event.
AU Rollini P; **Mach B**; Gorski J
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1985 Nov) 82 (21) 7197-201.
Journal code: PV3; 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198512
ED Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19851205
AB The predominant class II, or Ia, antigen of the human major histocompatibility complex is **HLA-DR**. It consists of an alpha and a beta chain, the latter being responsible for the remarkable polymorphism of these Ia antigens. Studies with cloned genes had shown the existence of more than one **DR** beta-chain locus. We have isolated about 100 kilobases of the **HLA-DR beta**-chain gene region from a cosmid library generated from a consanguineous homozygous B-cell line of the DR3 haplotype. Three **HLA-DR beta**-chain genes have been characterized. They are arranged in a head-to-tail orientation. One of the genes lacks the region encoding the first domain of the **DR** beta chain. The two other genes are transcribed, as shown by RNA blot hybridization analysis. A striking restriction site homology has been found within the **DR** beta-chain gene cluster, suggesting a recent duplication event involving at least 25 kilobases of DNA. Moreover, the molecular map of **DR** beta chain genes cloned from B-cell lines of two other **HLA-DR** haplotypes shows extensive homology between alleles of a given **DR** beta-chain locus.

L5 ANSWER 10 OF 14 MEDLINE
AN 86257409 MEDLINE
DN 86257409 PubMed ID: 3459965
TI Polymorphism of human Ia antigens: gene conversion between two **DR** beta loci results in a new **HLA**-D/**DR** specificity.
AU Gorski J; **Mach B**
SO NATURE, (1986 Jul 3-9) 322 (6074) 67-70.
Journal code: NSC; 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X04054; GENBANK-X04055; GENBANK-X04056; GENBANK-X04057; GENBANK-X04058; GENBANK-X04059
EM 198608
ED Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860815
AB The polymorphic **HLA-DR beta**-chains are encoded within the human major histocompatibility complex (MHC) by multiple loci resulting from gene duplications. Certain **DR** haplotypes can be grouped into families based on shared structural factors. We have studied the molecular basis of **HLA-DR** polymorphism within such a group which includes the haplotypes DR3, DR5 and DRw6. Molecular mapping of the **DR** beta-chain region allows true allelic comparisons of the two expressed **DR** beta-chain loci, **DR** beta I and **DR** beta III. At the more polymorphic locus, **DR** beta I, the allelic differences are clustered and may result from gene conversion events over very short distances. The gene encoding the **HLA**-DR3/Dw3 specificity has been generated by a gene conversion involving the **DR** beta I and the **DR** beta III loci of the **HLA**-DRw6/Dw18 haplotype, as recipient and donor gene, respectively. Based on which allele is found at **DR** beta III, the less polymorphic locus, two groups of haplotypes can be defined: DRw52a and DRw52b. The generation of **HLA-DR** polymorphism within the DRw52 supertypic group can thus be accounted for by a succession of gene duplication, divergence and gene conversion.

L5 ANSWER 9 OF 14 MEDLINE
AN 87133823 MEDLINE
DN 87133823 PubMed ID: 2434336
TI Immunochemical analysis of a cell transfected with an **HLA-DR** gene reveals a new alloantigenic specificity within **HLA**-DRw52.
AU Tosi R; Tanigaki N; De Preval C; Gorski J; **Mach B**
NC AI 20251 (NIAID)
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1986 Dec) 16 (12) 1603-8. Journal code: EN5; 1273201. ISSN: 0014-2980.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198703
ED Entered STN: 19900303
Last Updated on STN: 19970203
Entered Medline: 19870330
AB The **HLA-DR** antigen has been prepared from the surface of a mouse fibroblast cell line transfected with a single **HLA-DR beta**-chain gene as well as single **HLA-DR** alpha and invariant chain gene. Since the **HLA-DR beta** chain gene studied corresponds to the **DR** beta III locus, the **DR** serological specificities detected on the transformed cells can be assigned to this locus. The use of the **HLA-DR**-producing mouse cell line has led to the identification of a new serological specificity included within DRw52 and associated with some DR3, some DRw6 and all DR5 haplotypes studied. Most likely this new specificity corresponds to an allelic polymorphism at the **DR** beta III locus of DRw52 individuals and can serve as a new serological marker for this subset of DR3, DR5 and DRw6 haplotypes.

L5 ANSWER 6 OF 14 MEDLINE
AN 87248930 MEDLINE
DN 87248930 PubMed ID: 3596674
TI Structural comparison of the genes of two **HLA-DR** supertypic groups: the loci encoding DRw52 and DRw53 are not truly allelic.
AU Gorski J; Rollini P; **Mach B**
SO IMMUNOGENETICS, (1987) 25 (6) 397-402.
Journal code: GI4; 0420404. ISSN: 0093-7711.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198708
ED Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19870807
AB The organization and sequence of the **HLA-DR** **beta** chain genes are compared in the two supertypic groups, DRw52 and DRw53, which together account for more than 80% of **HLA-DR** alleles. From the structural data, we conclude that these two groups represent distinct lineages which have followed different patterns of evolution. The fine structure of the beta chain locus encoding the DRw53 specificity corresponds most closely to the **DR** beta II pseudogene in the DRw52 haplotypes. Concomitantly, the **DR** beta I locus in DRw53 haplotypes is more closely related to both of the two expressed **DR** beta loci of the DRw52 haplotypes (**DR** beta I and **DR** beta III). These two loci are the result of a recent duplication. This leads to the proposal that both expressed **DR** beta chain genes in the DRw52 haplotypes (**DR** beta I and **DR** beta III) are derived from a single precursor locus, while the two loci expressed in the DRw53 haplotypes are derived from distinct ancestral loci. The genes encoding DRw52 and DRw53 are therefore not true alleles of the same original locus. A scheme is proposed that accounts for the evolution of **DR** specificities within the DRw52 and DRw53 groups of haplotypes. It is evident that the different **HLA-DR** alleles are not structurally equidistant and that one must take into consideration different degrees of heterozygosity or mismatch among the **DR** alleles.

L5 ANSWER 4 OF 14 MEDLINE
AN 88006306 MEDLINE
DN 88006306 PubMed ID: 2820873
TI DNA typing of **HLA-DR beta** chain genes can discriminate between undetected alleles and real homozygotes.
AU de Preval C; Angelini G; Boogh B; Ferrara G B; **Mach B**
CS Department of Microbiology, School of Medicine, University of Geneva, Switzerland.
SO IMMUNOGENETICS, (1987) 26 (4-5) 249-57.
Journal code: GI4; 0420404. ISSN: 0093-7711.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198711
ED Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19871113
AB The polymorphism of **HLA-DR** antigens has been studied by Southern blot hybridization under conditions specific for the detection of the **DR** beta chain genes. Haplotype-specific patterns were defined with DNA from DR1, 2, 3, 4, 7, w8, w11, w12, and W13 homozygous typing cells, with restriction enzymes Eco RI, Bgl I, and Pvu II. Certain serological specificities, such as DR2, DR3, and DR7, can be encoded by distinct allelic forms of **DR** beta chain genes. The procedure of "DNA typing" was applied to family analysis of individuals expressing only a single **DR** specificity upon serological typing. Three cases are described here: (1) in family GR, phenotypic **DR** 7 homozygotes correspond to genomic heterozygotes, and a novel DR7 allele is described: (2) in family RU, the genes corresponding to a serologically undetected (blank) **DR** allele were identified by restriction fragment length polymorphism (RFLP); this novel **DR** haplotype has an RFLP pattern similar to those of the DRw52 family, even though this specificity was not expressed on the **DR**-blank lymphocytes; (3) in family RG, there is no blank allele, but a homozygote RFLP situation at the **DR** subregion.

TI Functional polymorphism of each of the two **HLA-DR** **beta** chain loci demonstrated with antigen-specific DR3- and DRw52-restricted T cell clones.

AU Irle C; Jaques D; Tiercy J M; Fuggle S V; Gorski J; Termijtelen A; Jeannet M; **Mach B**

CS Department of Medicine, Hopital Cantonal Universitaire, Geneva, Switzerland.

SO JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Mar 1) 167 (3) 853-72. Journal code: I2V; 2985109R. ISSN: 0022-1007.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198805

ED Entered STN: 19900308
Last Updated on STN: 19960129
Entered Medline: 19880502

AB **HLA**-DR3- and **HLA**-DRw52-associated functional polymorphism was investigated with selected tetanus toxoid (TT)-specific T cell clones. We have shown earlier that **HLA-DR** antigens are encoded by two distinct loci, **DR** beta I and **DR** beta III. The alloantigenic determinant(s) defined by the serological **HLA**-DR3 specificity map to the former, while the supratypic **HLA**-DRw52 determinants map to **DR** beta III. Furthermore, we have recently recognized by DNA sequencing three alleles of **HLA**-DRw52 at locus **DR** beta III, referred to as 52 a, b, and c. Our objective was to correlate the pattern of T cell restriction with the gene products of individual **DR** beta chain loci and with the three newly described alleles of locus **DR** beta III. Among the selected T cell clones, 5 reacted exclusively when TT was presented by **HLA**-DR3+ APCs (TT-DR3-APC). In contrast, two T cell clones were stimulated by TT-DRw52-APC. More specifically, these two T cell clones (Clones 10 and 16) were stimulated by different subsets of TT-DRw52-APC. Clone 16 responded to some DR3 and TT-DRw6-APC, while clone 10 was stimulated by other TT-DR3 and TT-DRw6, and all TT-DR5-APC. This same pattern of DRw52 restriction was found in panel, as well as in family studies. Because this suggested a correlation with the pattern of DRw52 polymorphism observed earlier by DNA sequencing and oligonucleotide hybridization, the APC used in these experiments were typed for the 52 a, b, and c alleles of locus **DR** beta III by allele-specific oligonucleotide probes. This distribution overlapped exactly with the stimulation pattern defined by the T cell clones. Clone 16 responded to TT-52a-APC, clone 10 to TT-52b-APC, and both clones to a TT-52c-APC. The response of the T cell clones was inhibited differentially by mAbs to **DR**. Raising TT concentration, or increasing **HLA**-class II expression with INF-gamma both affected the magnitude of response of the TT-specific clones but did not modify their specificities. These results demonstrate that a restriction specificity can be attributed to the **DR** beta III locus and illustrate the functional relevance of the polymorphism observed at this locus. This is of special interest in view of the striking difference in the pattern of structural diversity among alleles of **DR** beta I and **DR** beta III.

L5 ANSWER 2 OF 14 MEDLINE
AN 88243272 MEDLINE
DN 88243272 PubMed ID: 3132421
TI The single **DR** beta gene of the DRw8 haplotype is closely related to the **DR** beta 3III gene encoding DRw52.
AU Andersson G; Lindblom B; Andersson L; Gorski J; **Mach B**; Rask L
CS Department of Cell Research, Uppsala University, Sweden.
SO IMMUNOGENETICS, (1988) 28 (1) 1-5.
Journal code: GI4; 0420404. ISSN: 0093-7711.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198807
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880718
AB In most individuals two **HLA-DR beta** genes are expressed from each chromosome. One of these genes encodes one of the classical **DR** specificities, while the other encodes either of the supertypic DRw52/DRw53 specificities. In addition to these genes usually one or two **DR** beta pseudogenes are present. In contrast, the DRw8 chromosomal region only contains a single **DR** beta gene. To determine the relationship of this single gene to the multiple **DR** beta genes of other **DR** specificities, comparisons of Southern genomic blots were carried out. In this analysis genomic clones for each individual **DR** beta chain locus were included. The **DR** beta w8 gene was indistinguishable from the **DR** beta III gene of DR3 cells (encoding DRw52), suggesting that it is closely related to the latter gene. The functional implications of this finding are discussed.

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     FILE 'MEDLINE' ENTERED AT 11:20:50 ON 05 NOV 2001
                E MACH BF/AU
L1           250 S E1-E2
L2           124 S L1 AND HLA
L3            73 S L2 AND DR
L4             0 S L3 AND ((HLA)(W)(DR)(W)(BETA)(W)(B))
L5            14 S L3 AND ((HLA)(W)(DR)(W)(BETA))
L6             0 S L3 AND ((HLA)(W)(DR)(W)(B))
L7             0 S L1 AND HLA AND DRBA
L8           823 S HLA AND DR AND BETA AND (B)
L9             0 S HLA AND DR(W)BETA(W)B

=>
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